REMARKS

This responds to the Office Action mailed on November 1, 2006, and the references cited therewith.

No claims are amended, canceled, or added; as a result, claims 45-64 are now pending in this application.

§*103 Rejection of the Claims*

Claims 45-64 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Hill (WO 92/14472) and Gordon (Clinical Therapeutics, 1998; 20(1): 26-39) in view of Richards (U.S. Patent No. 4,985,418), and Budavari (Merck Index 11th ed. 1989, monograph 6021 and 7879) references of record in the parent application.

Applicants respectfully traverse the rejections, and request their reconsideration and withdrawal. For a claim to be rejected as obvious, the combination of references must disclose every claim element of the rejected claim, and, some teaching, suggestion or motivation must be found within the combination of references or within the knowledge of a person of ordinary skill that would lead the skilled artisan to combine the references to arrive at the claimed invention, and to have a reasonable expectation of success in doing so.

Applicants note that four separate documents are cited against the rejected claims. As each cited document discloses a spectrum of options which must be selected and combined to arrive at the claimed invention, in general it would seem that the motivation to combine all those particular elements in any particular combination must be more clearly indicated as the number of references increases.

Applicants respectfully submit that a *prima facie* case of obviousness has not been properly made by the Examiner. For the rejected claims, not every claim element is found in any of the combination of cited references. And, for the rejected claims, no teaching, suggestion or motivation to combine is found to arrive at the claimed invention.

The Examiner notes that Hill recites a composition comprising fluticasone propionate in combination with 10% of soft white paraffin, plus other ingredients. The Examiner also notes that Gordon recites a composition comprising another corticosteroid, clobetasol propionate, in an emollient cream. The emollient cream of Gordon is stated (page 28) to contain the silicone

dimethicone, which Gordon states acts "to occlude and protect the skin," i.e., as an occlusive, exerting the same skin-occlusive effect as does the soft white paraffin of Hill. Gordon does not recite any composition that lacks the occlusive agent dimethicone, nor does she state that the percentage of dimethicone used in her formulation is at anything below a usual level. The Examiner also notes that Gordon states that the absorption of steroids is greater when an occlusive agent is present in the formulation.

Applicants submit that independent claim 45 does not recite any compound serving an occlusive function, the claimed composition including: about 0.005 to 1.0 wt.% fluticasone, or a pharmaceutically acceptable salt or ester thereof; about 4.0 to 6.0 wt.% of a C_{14}-C_{20} fatty alcohol or mixtures thereof; about 1.0 to 5.0 wt.% of at least one first skin conditioning agent; about 5.0 to 15.0 wt.% propylene glycol; and the balance in water; wherein the lotion is free of mineral oil and white soft paraffin. The skin conditioning agent of claim 45 the present application is defined in the Specification to include compounds such as glycerine, isopropyl myristate, and lanolin alcohols, *inter alia*, but dimethicone is not included. The fact that Applicants do not view dimethicone as a skin conditioning agent is substantiated by Applicants' statement (page 3, line 31-32) in the original disclosure that a composition with a skin conditioning agent can in one embodiment *further contain* dimethicone, which is recited in claim 48 and claims dependent thereon. Thus, although Gordon refers to dimethicone as a "skin conditioner" (Table I), the Applicants herein do not define a "skin conditioning agent" as including dimethicone or any other skin-occlusive material. Therefore, claims 45, 46 and 47 cannot be obvious over the combination of documents cited by the Examiner, as the combination of references recites only combinations including an occlusive agent (soft white paraffin or dimethicone), wherein claim 45, and claims 46 and 47 dependent thereon, specifically exclude soft white paraffin and mineral oil, and do not recite or include dimethicone. Examples 2, 8, and 17 of the instant application provide inventive formulations that include no dimethicone or any other occlusive agent, providing support for compositions within claims 45-47 having a complete absence of dimethicone or any other occlusive agent such as soft white paraffin or mineral oil. Indeed, Applicants specifically note (page 1) that the instant composition exhibits unexpected vasoconstrictor potency with a reduced content of an occlusive agent. A reduced content of an

occlusive agent includes the absence of an occlusive agent, as shown in Examples, 2, 8, and 17, in instant claims 45-47.

None of the cited documents discloses a corticosteroid formulation for topical application that do not contain either soft white paraffin or dimethicone as an occlusive agent. Therefore, claims 45-47 cannot be obvious over these cited documents. Applicants accordingly request withdrawal of the rejections with respect to claims 45-47.

Concerning the other pending claims, instant claim 48 recites up to 5.0 wt% dimethicone, but claim 49 (dependent on claim 45), which is the basis of dependent claims 51-62, including method of treatment claims 61-62, recites 0.5 to 3.0 wt.% of dimethicone; thus, a maximum content of 3.0% dimethicone is incorporated in claims 51-62. Those instant Examples that include dimethicone mostly recite a level of 1.0-3.0%. In contrast, Hill recites a 10 wt% content of the occlusive agent soft white paraffin. Gordon recites no numerical content of her required occlusive agent dimethicone, but makes no indication that a "reduced" amount of dimethicone relative to levels typically used in the art is employed in her formulations.

Similarly, independent claims 63 and 64 recite, respectively, levels of dimethicone of up to 3.0%, and 1.0%. These values are well under the 10% recited by Hill for his occlusive ingredients, and are indicated in the instant application to be reduced levels, which Gordon does not disclose. Concerning the other two cited references, Richards does not involve topical application of fluticasone, only oral, stomal or rectal administration, and was cited by the Examiner on the issue of the preservative; Budavari (Merck Index) was cited specifically with regards to preservatives methyl and propyl paraben. These latter two documents are thus irrelevant on the issue of an occlusive agent in the composition.

None of the documents cited by the Examiner discloses the use of a reduced content of an occlusive agent relative to art contents, or levels of an occlusive agent of less than 10%. Thus, not all elements of claims 48-50, or of claims 51-62 dependent upon claims 49, are disclosed in the cited documents, and these claims cannot be obvious over those documents. Applicants accordingly request withdrawal of the rejections with respect to claims 48-62.

Similarly, all elements of independent claims 63 and 64 are not disclosed in the combination of documents cited by the Examiner, and cannot therefore be obvious over those

documents. Applicants accordingly request withdrawal of the rejections with respect to claims 63-64.

Gordon further states that clobetasol propionate is a "super high potency corticosteroid" (page 27), and also discusses at length the dangerous side effects that are associated with the use of high potency corticosteroids (page 27). In the instant application, the high potency corticosteroid formulations used for comparison (page 16, Table 2), Temovate® and Elocon®, contain clobetosol propionate and mometasone, respectively, not fluticasone. Fluticasone is found in the weaker control preparation Cutivate®, and hydrocortisone is found in Hytone®. Gordon states (page 28) that clobetasol propionate is some 1800 times more potent a corticosteroid than in hydrocortisone. It can therefore be inferred that fluticasone is less potent as a corticosteroid than is the super high potency clobetasol propionate.

A key, and surprising, feature of the present invention is the relatively high potency achieved by the inventive compositions comprising fluticasone relative to art fluticasone composition (Cutivate®). In the absence of an occlusive agent, or in the presence of an amount of an occlusive agent that is diminished relative to art levels, the present formulation provides for a higher potency than would be expected. As the Examiner notes, Gordon discloses that a higher corticosteroid potency for a given compound is typically observed in the presence of an occlusive agent. Therefore, it would not be obvious to remove or diminish the amount of an occlusive agent in order to confer enhanced potency on a less potent corticosteroid such as fluticasone.

As Hill's fluticasone formulation discloses high levels of occlusive agents, there would be no incentive or motivation found for the skilled artisan to include Gordon's dimethicone occlusive agents to Hill's already occlusive-rich formulation. Also, as Gordon reports superior results with her formulations using the high potency clobetasol propionate, the skilled artisan, searching for a better corticosteroid formulation, would find no incentive or motivation to substitute the weaker fluticasone of Hill for the more potent clobetasol of Gordon's formulation. Again, the Richards and Budavari documents are irrelevant on this topic.

Thus, an incentive, motivation, teaching or suggestion to combine these references would not be found in any of the cited documents, or in the knowledge of a person of ordinary skill. Therefore, with respect to all pending claims 45-64, no *prima facie* case of obviousness has

properly been made. Applicants accordingly request withdrawal of all the rejections made on this basis.

CONCLUSION

Applicant respectfully submits that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney at (612) 373-6941 to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

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Date Feb. 1, 2007

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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Mail Stop Amendment, Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 1st day of February, 2007.

PATRICIA A. HULTMAN

Name

Signature